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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,874	02/06/2001	Iris Pecker	01/21603	8407

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EXAMINER

HUTSON, RICHARD G

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/776,874	PECKER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2006.
- 2a) ☒ This action is **FINAL**.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 97-101 and 123-129 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 129 is/are allowed.
- 6) ☒ Claim(s) 97-99 and 123-126 is/are rejected.
- 7) ☒ Claim(s) 100, 101, 127 and 128 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's amendment of claims 97, 123, 125, cancellation of claims 119-122 and the addition of new claims 128 and 129, in the paper of 8/6/2006, is acknowledged.

Claims 97-101 and 123-129 are at issue and are present for examination.

Applicants' arguments filed on 8/2/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Objections***

Claims 100, 101, 127, 128 are objected to because of the following informalities:

Claims 100, 101, 127, 128 are dependent on rejected claim 97.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 97-99 and 123-126 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein or preparation comprising said protein having the amino acid sequence of SEQ ID NO: 10, said protein having

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heparanase activity or being so cleavable so as to acquire said heparanase activity, does not reasonably provide enablement for any protein or preparation comprising said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, wherein said protein is merely 70% homologous to SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was originally stated in the previous office actions as it applied to previous claims 97-99 and 123-126. In response to this rejection applicants have amended claims 97, 123, 125, canceled claims 119-122 and added new claims 128 and 129 and traverse the rejection as it applies to the new claims.

As an initial matter applicants question the inclusion of claims 123-126 in the current rejection. Applicants submit that based on the actions enablement position, these claims should be withdrawn from the rejection. The enablement rejection has been reviewed, and it is not believed that these claims necessitate their removal based upon this position. As applicants have not specifically pointed out why these specific claims should be considered separately from the remaining claims, this issue is not further considered.

Applicants continue to traverse the rejection on the basis that the decision of the Board of Patent Appeals and Interferences in *Ex Parte Sun* dictates a finding of enablement in the instant invention.

Applicants acknowledge the previous examiner's statements that "the factors necessary for the determination of the enablement of the instant claims and that of the referred to decision are different, however, applicants assert that nowhere is it stated "How they are different and why this difference makes a difference in finding enablement of the claims in Sun, but not in the instant application."

Applicants further submit that in Sun, claims to 80% homology were found to be enabled, in contrast to 80% and 90% homology claimed here. As previously stated, the factors necessary for the determination of the enablement of the instant claims and that of the referred to board decision are different. For applicants convenience it is pointed out to applicants that the referred to claims from *Ex parte Sun* are drawn to a wee1 'polynucleotide' having at least 80% identity to the entire coding region of SEQ ID NO: 1 and this is a 403 amino acid encoding polynucleotide. The instant claims are drawn to a "preparation comprising a heparanase protein" said heparanase having at least 80% homology to SEQ ID NO: 10, wherein said heparanase is pure enough to elicit anti-heparanase antibodies.

While the examiner has not presented an exhaustive list comparing each of the Wands factors for the instant claims and that of *Ex parte Sun*, applicants have neither pointed out similarities between the two decisions beyond that the each encompasses a percent homology or identity and a protein or polynucleotide. Thus the current claims remain rejected under a lack of enablement, for the reason previously stated and of record.

The specification does not support the broad scope of the claims which encompass the claimed preparations comprising a heparanase protein, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting heparanase activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the heparanase activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus.

While applicants have provided some guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those number of amino acid modifications of any heparanase having 95% homology to SEQ ID NO: 10, applicants have not provided sufficient guidance to enable those variants having a mere 70 % homology to SEQ ID NO: 10, for the reasons previously presented.

As previously stated, current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would not allow for finding the few active mutants within

the several hundred thousand to greater than several trillions of inactive mutants, as is the case for the claims limited to 70% identity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any heparanase having a mere 70% homology to SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those preparations having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 97-101 and 123-126 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al. (U.S. Patent No. 5,362,641).

The rejection was originally stated in the previous office actions 10/3/2005 as it applied to previous claims 97-101 and 119-127. In response to this rejection applicants have amended claims 97, 123, 125, canceled claims 119-122 and added new claims 128 and 129 and traverse the rejection as it applies to the new claims.

As an initial matter applicants question the rejection with respect to claim 127. Applicant's statements of the issue with respect to claim 127 is acknowledged, and claim 127 is hereby withdrawn from the rejection.

Applicants continue to argue on the basis that the preparation of Fuks et al. cannot or does not elicit antibodies against heparanase. Applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found non-persuasive on the following basis.

As previously stated, the preparation taught by Fuks et al. is that of an isolated heparanase, from the same source as applicants claimed heparanase and thus Fuks et al. continues to make obvious applicants claimed isolated heparanase protein for all of the reasons of record. Applicants comments that applicants are not (merely) claiming "an isolated heparanase" but rather a heparanase protein "that is pure enough to elicit anti-heparanase antibodies" is acknowledged and it continues to be the position of the office that the "heparanase" protein taught by Fuks et al. "is pure enough to elicit anti-heparanase antibodies" even if the heparanase protein taught by Fuks et al. was in a



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composition that "did not elicit anti-heparanase antibodies". The limitation/characteristic that the heparanase of the claimed invention "is pure enough to elicit anti-heparanase antibodies" is an inherent limitation/characteristic of the isolated heparanase taught by Fuks et al.

Thus claims 97-101 and 123-126 remain anticipated by Fuks et al.

***Remarks***

No claim is allowed.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Richard G. Hutson', with a long horizontal line extending to the right.

Richard G Hutson, Ph.D.  
Primary Examiner  
Art Unit 1652

rg  
4/4/2006